07/003,822
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L1 STRUCTURE CREATED

=> DIS L1 QUE
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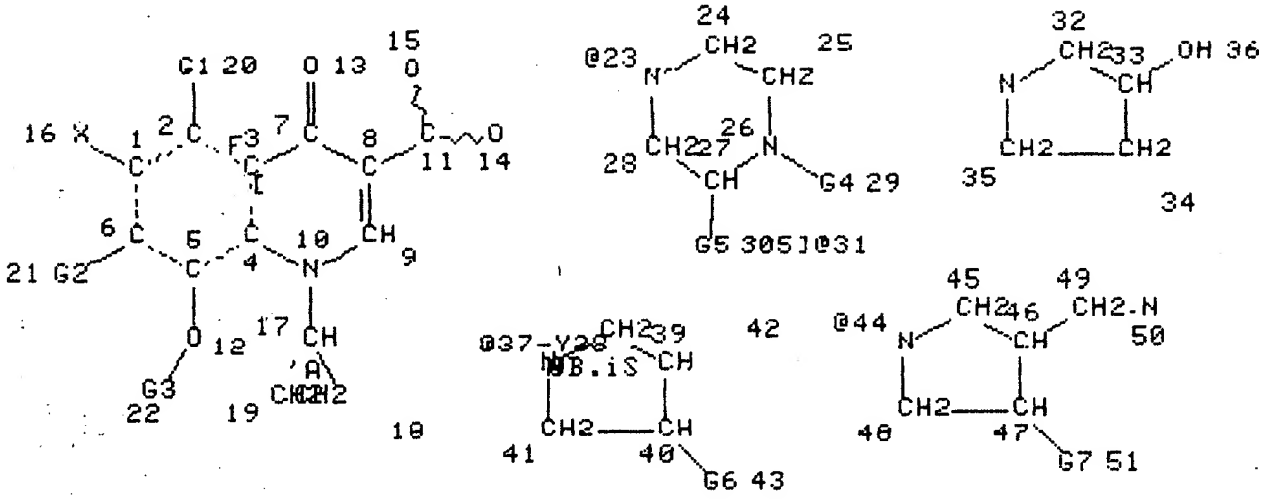

VAR G1=H/NH2/NO2
VAR G2=X/23/31/37/44
VAR G3=ME/ET/N-PR/I-PR/N-BU/S-BU/I-BU/T-BU
VAR G4=H/ME
VAR G5=H/ME
VAR G6=H/ME/ET/N-PR/I-PR/N-BU/S-BU/I-BU/T-BU
VAR G7=H/ME/ET/N-PR/I-PR/N-BU/S-BU/I-BU/T-BU
NODE ATTRIBUTES:
NSPEC IS C AT 42
NSPEC IS C AT 50

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 51

=> S L1 FUL
FULL SEARCH INITIATED 11:11:38
SCREENING
FULL SCREEN SEARCH COMPLETED - 65 TO ITERATE
100.0% PROCESSED 65 ITERATIONS 49 ANSWERS
SEARCH TIME: 00.00.30

L2 49 SEA SSS FUL L1

=> FILE CA
FILE 'CA' ENTERED AT 11:12:26 ON 08 JAN 90
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE COVERS 1967 - 6 JAN 90 (900106/ED) VOL 112 ISS 02.
For OFFLINE Prints or Displays, use the ABS or ALL formats
to obtain abstract graphic structures. The AB format DOES
NOT display structure diagrams.

=> S L2
L3 5 L2

=> DIS L3 1-5 ALL

L3 ANSWER 1 OF 5
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AN CA111(13):114845v
TI Preparation of fluoroanisole derivatives as intermediates for fluoroquinolone antibacterials
AU Masuzawa, Kuniyasu; Suzue, Seigo; Hirai, Keiji; Ishizaki, Takayoshi
CS Kyorin Pharmaceutical Co., Ltd.
LO Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
PI JP 01016746 A2 20 Jan 1989 Heisei
AI JP 87-171946 9 Jul 1987
IC ICM C07C059-90
ICS C07C051-06; C07C051-353; C07C051-60; C07C065-21; C07C069-738; C07C102-08; C07C103-26; C07C121-75; C07D215-56
SC 25-9 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
SX 1
DT P
CO JKXXAF
PY 1989
LA Japan
GI

L3 ANSWER 1 OF 5
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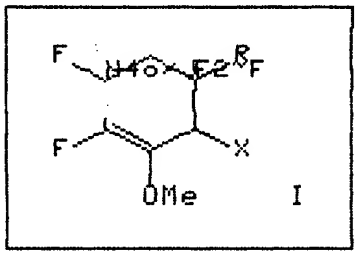

I

AB The title compds. I (R = CN, CONH2, CO2H, COCl, COCH2CO2R1; R1 = H, lower alkyl; X = halo), useful as intermediates for fluoroquinolone antibacterials, were prepd. A mixt. of 3-bromo-2-chloro-5,6-difluoroanisole and CuCN in N-methyl-2-pyrrolidone was stirred at 130.degree. for 5 h to give 2-chloro-4,5-difluoro-3-methoxybenzonitrile.
KW fluoroanisole prepn fluoroquinolone antibacterial intermediate; anisole fluoro prepn antibacterial intermediate
IT Bactericides, Disinfectants, and Antiseptics
(intermediates for, prepn. of fluoroanisoles as)
IT 66684-55-7P 112811-66-2P 112811-67-3P ***112811-73-1P***
122375-82-0P 122375-83-1P 122375-84-2P 122375-85-3P
122375-86-4P 122375-87-5P 122375-88-6P 122375-89-7P
122375-90-0P 122375-91-1P
(prepn. and reaction of, in prepn. of bactericide)
IT ***112811-57-1P*** ***112811-58-2P*** ***112811-59-3P***
112811-61-7P ***112811-62-0P*** 122394-84-7P

L3 ANSWER 1 OF 5
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(prepn. of, as antibacterial)
IT 112811-63-9P 112811-64-0P 112811-65-1P 112811-68-4P
112811-71-9P ***112811-72-0P*** 122375-78-4P
122375-79-5P 122375-80-8P 122375-81-9P
(prepn. of, as intermediate for fluoroquinolone antibacterial)
IT 105-53-3, Diethyl malonate 109-01-3, N-Methylpiperazine
109-07-9, 2-Methylpiperazine 110-85-0, Piperazine, reactions
122-51-0, Triethyl orthoformate 551-62-2,
1,2,3,4-Tetrafluorobenzene 765-30-0, Cyclopropylamine 3862-73-5,
2,3,4-Trifluoroaniline 99724-19-3 107610-69-5 107610-73-1
122375-79-5 122375-81-9
(reaction of, in prepn. of intermediate for antibacterial fluoroquinolones)
IT 544-92-3, Copper(I) cyanide
(reaction of, with bromobenzene deriv.)

L3 ANSWER 2 OF 5
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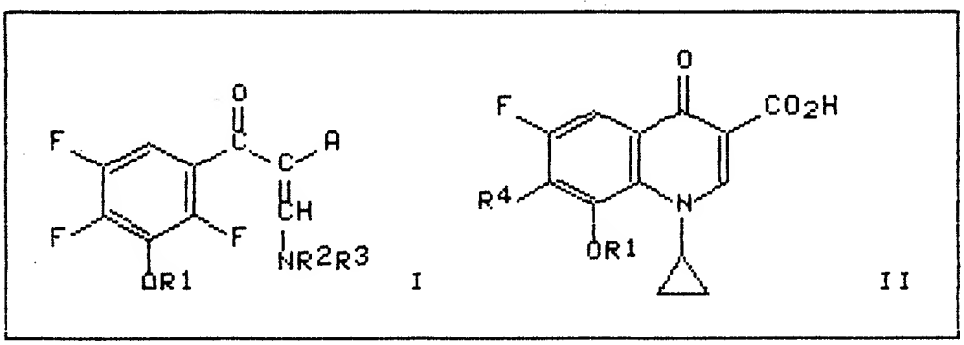
AN CA111(11):97105j
TI Preparation of 3-am[illegible]-2-(3-alkoxy-2,4,5-triflu[illegible]benzoyl)acrylic acid derivatives as intermediates for antibacterials
AU Ataka, Kikuo; Oku, Masayoshi; Omori, Kiyoshi; Kimura, Tomio; Iwata, Masayuki
CS Ube Industries, Ltd.; Sankyo Co., Ltd.
LO Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
PI JP 63316757 A2 26 Dec 1988 Showa
AI JP 87-152099 18 Jun 1987

L3 ANSWER 2 OF 5

IC ICM C07C101-34
ICS C07C099-00; C07C121-78; C07D295-00; C07D295-14
ICA A61K031-215; A61K031-275
SC 27-17 (Heterocyclic Compounds (One Hetero Atom))
SX 1, 25, 28
DT P
CO JKXXAF
PY 1988
LA Japan
GI



AB The title compds. (I; R1 = lower alkyl; R2,R3 = alkyl; or NR2R3 = cyclic amino optionally contg. O, S, SO, or SO2; A = cyano, lower alkoxycarbonyl) useful as intermediates for antibacterial

L3 ANSWER 2 OF 5

quinolonecarboxylic acids (II; R4 = 1-pyrrolidinyl or 4-piperazinyl optionally substituted by lower alkyl, lower alkoxy, OH, or NH2), were prepd. A soln. of Me2NCH:CHCO2Et in THF was added dropwise under ice-cooling, followed by Et3N, to a soln. of 3-methoxy-2,4,5-trifluorobenzoyl chloride (III) in THF. The mixt. was stirred 5 h at room temp. and left to stand overnight to give 29% I (R1-R3 = Me, A = CO2Et) which was treated with cyclopropylamine in CH2Cl2 to give I (R1 = Me, NR2R3 = cyclopropylamino, A = CO2Et). A soln. of the latter in THF contg. NaH was stirred 30 min at room temp. to give II (R1 = Me, R4 = F) Et ester which was treated with 42% HBF4 to give II.BF2 (R1 = Me, R4 = F). The latter and piperazine were reacted overnight at room temp. in Me2SO to give II (R4 = 1-piperazinyl, R1 = Me)(IV). IV exhibited min. inhibitory concns. of .ltoreq.0.01 to 0.8 .mu.g/mL against 14 bacteria (e.g. Staphylococcus aureus and Escherichia coli).
KW aminobenzoylacrylate prepn intermediate antibacterial quinolonecarboxylate
IT Bactericides, Disinfectants, and Antiseptics
(quinolonecarboxylates, intermediates for, aminobenzoylacrylates as)
IT 110-85-0, Piperazine, reactions
(amination by, of difluoroquinoline carboxylic acid deriv.)
IT 765-30-0, Cyclopropylamine
(amine exchange of, with Me(dimethylamino)acrylate deriv.)
IT 924-99-2, Ethyl 3-(dimethylamino)acrylate 999-59-7, Methyl 3-(dimethylamino)acrylate 2407-68-3, 3-(Dimethylamino)acrylonitrile
(condensation of, with methoxytrifluorobenzoyl chloride)
IT 151-50-8, Potassium cyanide

L3 ANSWER 2 OF 5

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(cyanation by, of diazotized methoxytrifluroaniline)
IT 773-82-0, Pentaflurobenzonitrile
(methoxylation of, by sodium methoxide)
IT 115685-58-0P
(prepn. and amination of, by piperazine)
IT 5291-88-3P, 4-Methoxy-2,3,5,6-tetrafluorobenzonitrile
(prepn. and ammonolysis of)
IT 112811-66-2P, 3-Methoxy-2,4,5-trifluorobenzoyl chloride
(prepn. and condensation of, with Me(dimethylamino)acrylate)
IT 112811-65-1P, 3-Methoxy-2,4,5-trifluorobenzoic acid
(prepn. and conversion of, to acid chloride)
IT 112811-70-8P
(prepn. and cyclization of)
IT 114214-46-9P
(prepn. and decyanation of)
IT ***112811-71-9P***
(prepn. and deethylation of)
IT 114214-45-8P, 3-Methoxy-2,4,5-trifluoroaniline
(prepn. and diazotization-cyanation of)
IT 112811-63-9P, 3-Methoxy-2,4,5-trifluorobenzonitrile 112811-64-0P, 3-Methoxy-2,4,5-trifluorobenzamide
(prepn. and hydrolysis of)
IT ***112811-57-1P*** ***114213-75-1P*** ***114213-76-2P*** ***114213-92-2P*** 121577-31-9P ***121577-32-0P*** ***121577-33-1P***
(prepn. of, as antibacterial)
IT 121577-34-2P 121577-35-3P 121577-36-4P 121577-37-5P
(prepn. of, as intermediate for antibacterial

L3 ANSWER 2 OF 5
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L3 ANSWER 3 OF 5
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AN CA110(15):135095v
TI Preparation of alkoxyfluoroquinolonecarboxylic acid derivatives as medical bactericides
AU Iwata, Masayuki; Kimura, Tomio; Fujiwara, Yoshimi; Katsube, Tetsushi
CS Sankyo Co., Ltd.; Ube Industries, Ltd.
LO Japan
SO Eur. Pat. Appl., 188 pp.
PI EP 241206 A2 14 Oct 1987
DS R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
AI EP 87-302813 31 Mar 1987
PRAI JP 86-74064 31 Mar 1986
JP 86-225120 24 Sep 1986
JP 86-313852 24 Dec 1986
IC ICM C07D215-56
ICS C07D401-04; A61K031-47; A61K031-495; A61K031-535; A61K031-54; A61K031-55
ICA C07D209-48; C07C093-14; C07C121-75; C07C063-70; C07C121-78; C07C103-22; C07C069-738; C07D207-14
SC 27-17 (Heterocyclic Compounds (One Hetero Atom))
SX 1
DT P
CO EPXXDW
PY 1987
LA Eng
11:21:10 COPY AND CLEAR PAGE. PLEASE

L3 ANSWER 3 OF 5
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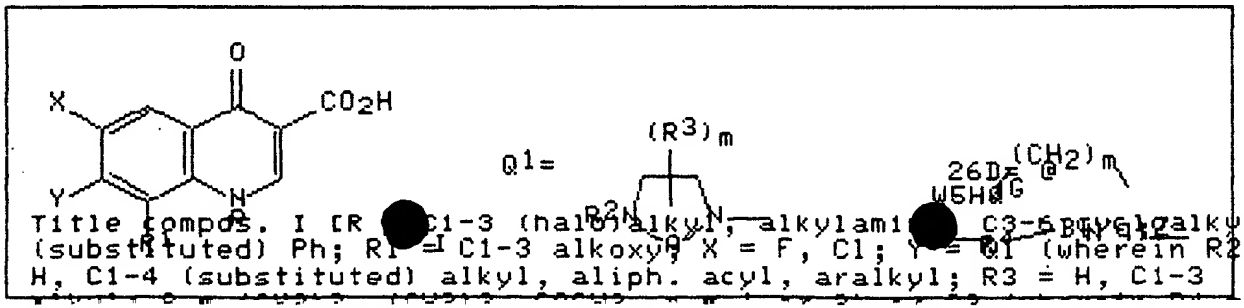
GI



AB Title compds. I [R = C1-3 (halo)alkyl, alkylamino, C3-6 cycloalkyl, (substituted) Ph; R1 = C1-3 alkoxy; X = F, Cl; Y = Q1 (wherein R2 = H, C1-4 (substituted) alkyl, aliph. acyl, aralkyl; R3 = H, C1-3

C1-3 alkyl, OH, C1-3 alkoxy; W = OH, C1-3 alkoxy, etc.; B = (CH2)2, (CH2)3; m = as given above)], useful as antibacterials, were prepd. A mixt. of 0.11 g 1-cyclopropyl-6,7-difluoro-8-methoxy-1,4-dihydro-4-oxoquinoline-3-carboxylic acid boron difluoride chelate (prepn. given) and 0.11 g piperazine in 0.5 mL Me2SO was allowed to stand at room temp. overnight and then poured into Et2O. Crystals were collected by filtration and dissolved in 30 mL 80% aq. EtOH and 5 mL Et3N. The resulting soln. was refluxed for 4 h and worked up to give I.cntdot.HCl (X = F, Y = 1-piperazinyl, R1 = MeO, R = cyclopropyl)

L3 ANSWER 3 OF 5
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(II). II in vitro exhibited a MIC of 0.1 .mu.g/mL against Staphylococcus aureus 209P.
KW quinolonecarboxylate alkoxyfluoro prepn medical bactericide; bactericide medical alkoxyfluoroquinolonecarboxylate prepn
IT Bactericides, Disinfectants, and Antiseptics
(alkoxyfluoroquinolonecarboxylic acid derivs.)
IT 109-01-3, N-Methylpiperazine 110-85-0, Piperazine, reactions 110-91-8, Morpholine, reactions 40499-83-0, 3-Hydroxypyrrolidine
(amination by, of difluoroquinolone deriv.)
IT ***112811-59-3P***
(prepn. and methylation of)
IT 114214-23-2P
(prepn. and reaction of, in prepn. fluoroquinolone bactericide)
IT 114213-93-3P, cis-3-Amino-4-methoxypyrrolidine
(prepn. and reaction of, with difluoroquinolonecarboxylic acid deriv.)
IT 112282-60-7P ***112811-57-1P*** ***112811-58-2P***
112811-59-3P ***112811-60-6P*** ***112811-74-2P***
112811-76-4P ***112811-81-1P*** ***114213-69-3P***
114213-70-6P 114213-71-7P 114213-72-8P ***114213-73-9P***

L3 ANSWER 3 OF 5
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dihydrochloride 114214-54-9P 114214-55-0P 114214-56-1P
114214-57-2P 114214-58-3P 114214-59-4P 114214-60-7P
114214-61-8P 114214-62-9P 114214-63-0P 114214-64-1P
114214-65-2P 114214-66-3P 114214-67-4P 114214-68-5P
114214-69-6P 114214-70-9P 114214-71-0P 114214-72-1P
114214-73-2P 114214-74-3P, 3-Amino-4-methylpyrrolidine dihydrochloride
(prepn. of, as intermediate in prepn. of fluoroquinolone bactericide)
IT 97-63-2, Ethyl methacrylate 105-36-2, Ethyl bromoacetate 1074-82-4, Potassium phthalimide 5731-17-9 82419-26-9, 2,3-Difluoro-6-nitrophenol 114214-52-7
(reaction of, in prepn. of fluoroquinolone bactericide)

L3 ANSWER 4 OF 5
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AN CA109(11):92826u
TI Antibacterial substituted-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acids, substituted-9-fluoro-3-methyl-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acids, derivatives thereof, pharmaceutical compositions comprising the compounds, and processes for producing the compounds
AU Domagala, John Michael; Mich, Thomas Frederick; Sanchez, Joseph Peter
CS Warner-Lambert Co.
LO USA
SO Eur. Pat. Appl., 35 pp.

L3 ANSWER 4 OF 5
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY
PI EP 265230 A1 27 Apr 1988
DS, LB; NBT,SBE, CH, DE, ES, FR, GB, GR, IT,
AI EP 87-309267 20 Oct 1987
PRAI US 86-920536 20 Oct 1986
IC ICM C07D401-04
ICS C07D498-06; C07D471-04; A61K031-47; A61K031-535
SC 27-17 (Heterocyclic Compounds (One Hetero Atom))
SX 1 28

US 4,822,801
514/312

DT P
CO EPXXDW
PY 1988
LA Eng
GI For diagram(s), see printed CA Issue.
AB The title compds. I and II [Z = Q, etc.; Y = NH2, NHR, NRR', OR, OH; R, R' = C1-6 alkyl, C3-16 cycloalkyl; X = CH, CF, CCl, CBr, COR, COH, CCF3, N; n = 1-4; m = 1-4; n + m = 2-5; l = 0-2; R1 = H, C1-6 alkyl, cation; R2 = C1-4 alkyl, vinyl, haloalkyl, hydroxyalkyl, cycloalkyl; R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C2-4 hydroxyalkyl, R7CO, etc.; R5, R6 = H, C1-3 alkyl; R7 = C1-4 alkyl, alkoxy; R8 = H, lower alkyl; with the provisios that: (a) when Y = NH2, X is not CH or N; and (b) when Y is NH2 and R2 is alkyl, vinyl, haloalkyl, hydroxyalkyl, X is not CF], useful as antibacterials (no data), were prepd. Reaction of 1-ethyl-5-amino-6,7,8-trifluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (prepn. given) with 3-(tert-butoxycarbonylamino)pyrrolidine, followed by deprotection, gave I.cntdot.HCl [R1 = H, R2 = Et, Y = NH2, Z = (3-amino-1-pyrrolidinyl), X = CF].
KW quinolonecarboxylate amino prepn antibacterial;
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L3 ANSWER 4 OF 5
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114373-12-5P 114373-13-6P 114373-14-7P 115904-52-4P
115904-53-5P 115904-54-6P 115904-55-7P 115904-56-8P
(prepn. of, in prepn. of antibacterial quinolones)
IT 87-13-8, Diethyl (ethoxymethylene)malonate 105-53-3 765-30-0, Cyclopropylamine 1071-46-1, Malonic acid monoethyl ester 5733-86-8 15568-85-1 16583-08-7, 2-Nitro-3,4-5,6-tetrafluorobenzoic acid 18471-40-4 38512-77-5, 2-Methoxy-3,4,5,6-tetrafluorobenzoic acid 51535-00-3 67852-79-3, Sodium 2,3,4,5-tetrafluorobenzoate 75167-21-4 79660-46-1 84427-35-0 91187-83-6, 3-(Ethylaminomethyl)pyrrolidine 91187-89-2, N-Cyclopropyl-3-pyrrolidinemethanamine 91189-23-0 99724-19-3, 3-(tert-Butoxycarbonylamino)pyrrolidine 99735-37-2 101513-77-3, 3-Chloro-2,4,5-trifluorobenzoic acid 103772-14-1 111230-53-6
(reaction of, in prepn. of antibacterial quinolones)

L3 ANSWER 5 OF 5
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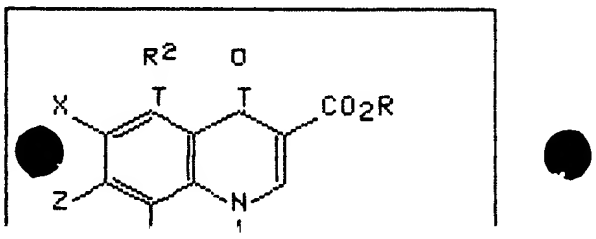
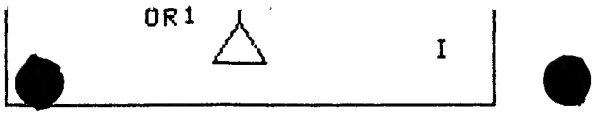
AN CA108(9):75230g
TI Preparation of 8-alkoxyquinolonecarboxylic acids as antibacterials with selective toxicity
AU Masuzawa, Kuniyoshi; Suzue, Seigo; Hirai, Keiji; Ishizaki, Takayoshi
CS Kyorin Pharmaceutical Co., Ltd.
LO Japan
SO Eur. Pat. Appl., 44 pp.
PI EP 230295 A2 29 Jul 1987
DS R: BE, CH, DE, FR, GB, IT, LI, NL, SE
AI EP 87-100608 19 Jan 1987

L3 ANSWER 5 OF 5
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY
PRAI JP 86-10880 21 Jan 1986
JP 86-220149 18 Sep 1986
IC ICM C07D215-56
ICS C07D401-04; A61K031-47
SC 27-17 (Heterocyclic Compounds (One Hetero Atom))
SX 1
DT P
CO EPXXDW
PY 1987
LA Eng
GI





AB The title compds. I (R = H, alkyl; R1 = alkyl; R2 = H, NH2, NO2; X = halo; Z = halo, piperazino, N-methylpiperazino, 3-methylpiperazino,

L3 ANSWER 5 OF 5

3-hydroxypyrrolidino, etc.), useful as antibacterials, were prepd. A mixt. of 200 mg 1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylic acid and 180 mg piperazine in 3 mL DMSO was stirred for 2.5 h at 70-80.degree. to give 40 mg 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid (II). II in vitro exhibited a MIC of 0.10 .mu.g/mL against Staphylococcus aureus 209 P.

KW quinolonecarboxylate alkoxyfluoro prepn medical bactericide; bactericide medical alkoxyfluoroquinolonecarboxylate prepn

IT Bactericides, Disinfectants, and Antiseptics
(medical, alkoxyquinolonecarboxylic acid derivs.)

IT 109-01-3, N-Methylpiperazine 109-07-9, 2-Methylpiperazine 110-85-0, reactions 67318-88-1, 3-Aminomethylpyrrolidine 91187-81-4, 3-Methylaminomethylpyrrolidine 91187-83-6, 3-Ethylaminomethylpyrrolidine 99724-19-3, 3-tert-Butoxycarbonylaminopyrrolidine 107610-69-5 107610-73-1
(amination by, of difluoroquinolonecarboxylic acid deriv.)

IT 551-62-2
(bromination and methoxylation of)

IT 94242-53-2 99734-96-0 99734-98-2 103460-89-5 112811-82-2
(methoxylation of)

IT ***112811-78-6P***
(prepn. and amination of)

IT ***112811-72-0P***
(prepn. and amination or nitration of)

IT 112811-68-4P
(prepn. and condensation of, with Et orthoformate)

IT 112811-66-2P

L3 ANSWER 5 OF 5
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(prepn. and condensation of, with di-Et malonate)

IT 13332-24-6P
(prepn. and cyanation of)

IT 112811-70-8P
(prepn. and cyclocondensation of)

IT 112811-67-3P
(prepn. and decarboxylation of)

IT ***112811-62-8P*** ***112811-73-1P***
(prepn. and deprotection of)

IT 112811-63-9P ***112811-71-9P***
(prepn. and hydrolysis of)

IT 112811-69-5P
(prepn. and reaction of, with cyclopropylamine)

IT 112811-65-1P
(prepn. and reaction of, with thionyl chloride)

IT ***112811-77-5P***
(prepn. and redn. of)

IT 99734-98-2P ***112811-57-1P*** ***112811-58-2P***
112811-59-3P ***112811-60-6P*** ***112811-61-7P***
112811-62-8P ***112811-74-2P*** 112811-75-3P
112811-76-4P ***112811-79-7P*** ***112811-80-0P***
112811-81-1P ***112811-83-3P***
(prepn. of, as antibacterial agent)

IT 112811-64-0P, 2-Methoxy-2,4,5-trifluorobenzamide
(prepn. of, as intermediate in prepn. of fluoroquinolone antibacterial agent)

IT 765-30-0, Cyclopropylamine

=> LOG Y
STN INTERNATIONAL LOGOFF AT 11:33:19 ON 08 JAN 90